Assignment of the TIMP gene to the murine X-chromosome using an inter-species cross

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Assignment of the TIMP gene to the murine X-chromosome using an inter-species cross

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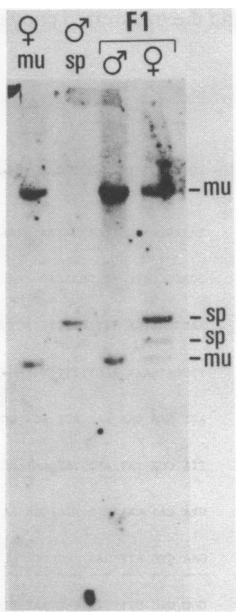
The glycoprotein tissue inhibitor of metalloproteinases (TIMP) is a physiological inhibitor of collagenase, stromelysin and gelatinase, which are thought to be involved in extracelluar matrix turnover (1). It inhibits to a lesser extent the PMN leucocyte metalloproteinases (1). The gene for human TIMP has been cloned (2), and it was shown to be identical to a cDNA previously identified as erythroid potentiating activity. This human gene has been mapped to the X-chromosome (3,4). We have isolated the mouse TIMP gene from an embryonic cDNA library (provided by Dr. Brigid Hogan) by cross-hybridisation to the human gene. DNA sequencing of the mouse coding sequence shows it to have 72% amino-acid identity with its human counterpart (T.D. Le Cras, unpublished).

Linkage of particular genes to the X-chromosome is conserved throughout the mammals. We therefore anticipated X-linkage of the mouse TIMP gene. To establish this linkage we utilised a cross between two mouse species, *M. musculus* and *M. spretus*. As the two species are 4-5 million years diverged, almost all DNA probes reveal a difference in restriction fragment length after gel electrophoresis and Southern blot hybridisation. The Figure shows that the mouse TIMP probe identifies 2 fragments in EcoR1-digested DNA from *M. musculus* (labelled **mu**) and two different fragments in *M. spretus* DNA (**sp**). Hybridisation to EcoR1 digested DNA from male and female F1 offspring of a cross between a male *M. spretus* and a female *M. musculus* is shown. The female offspring inherits the fragments from both parents, whilst the male offsring inherits only the maternal (*musculus*) fragments. This clearly demonstrates the the TIMP gene is on the murine X-chromosome, and has no cross-hybridising homologues on the Y-chromosome or the autosomes.



This method is generally applicable and provides a rapid means of demonstrating X-linkage of any DNA probe.

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